



#6

09892613.ST25

SEQUENCE LISTING

<110> Leung, Shawn Shui-on

<120> REDUCING IMMUNOGENICITIES OF IMMUNOGLOBULINS BY FRAMEWORK-PATCHING

<130> 655

<140> US 09/892,613

<141> 2001-06-27

<160> 32

<170> PatentIn version 3.1

<210> 1

<211> 369

<212> DNA

<213> Artificial Sequence

<220>

<223> FR-patched heavy chain variable region sequence (Full DNA Sequence) formed by joining the N- and C- terminal (SEQ 3 and 6) halves at the KpeI site.

<220>

<221> V_region

<222> (1)..(369)

<223>

<400> 1

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gaagtgcagc tgctggagtc tgggggaggc ttagtgcagc ctggagggtc cctgaggctc      60
tcctgtgcag cctctggatt ctccttcagt atctatgaca tgtcttgggt tcgccaggca      120
ccgggaaagg ggctggagtg ggtcgcatat attagtagtg gtggtggtac cacctactat      180
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ccagacactg tgaagggccg attcaccatc tccagagaca atgccaagaa ctccctgtac 240
 ctgcaaata acagtctgag ggtggaggac acagccttat attactgtgc aagacatagt 300
 ggctacggtg gtagctacgg ggttttgttt gcttactggg gccaaaggac tctggtcact 360
 gtctctttca 369

<210> 2

<211> 123

<212> PRT

<213> Chimaera sp.

<400> 2

Glu Val Gln Leu Leu Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
 1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Ser Phe Ser Ile Tyr
 20 25 30

Asp Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
 35 40 45

Ala Tyr Ile Ser Ser Gly Gly Gly Thr Thr Tyr Tyr Pro Asp Thr Val
 50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr
 65 70 75 80

Leu Gln Met Asn Ser Leu Arg Val Glu Asp Thr Ala Leu Tyr Tyr Cys
 85 90 95

Ala Arg His Ser Gly Tyr Gly Ser Ser Tyr Gly Val Leu Phe Ala Tyr
 100 105 110

Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser
 115 120

<210> 3

<211> 111

<212> DNA

<213> Artificial Sequence

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<220>

<223> N-template is a synthetic sense-strand oligonucleotide encoding a
mino acids 14-50 of the VH region (SEQ ID No. 2). The template is
PCR-amplified by two primers (SEQ ID No. 4 and 5)

<220>

<221> V_region

<222> (1)..(111)

<223>

<400> 3
cctggagggg ctctgaggct ctctgtgca gcctctggat tctccttcag tatctatgac 60
atgtcttggg ttgccaggc accgggaaag gggctggagt gggtcgcata c 111

<210> 4

<211> 57

<212> DNA

<213> Artificial Sequence

<220>

<223> 5' Primer is a synthetic sense-strand oligonucleotide encoding am
ino acid 1-19 of the VH region (SEQ ID No. 2). The 3' end of the
primer overlaps with the 5' end of the template by 18 nucleotides

<220>

<221> primer_bind

<222> (1)..(57)

<223>

<400> 4
gaagtgcagc tgctggagtc tgggggaggc ttagtgcagc ctggaggggc cctgagg 57

<210> 5

<211> 48

<212> DNA

<213> Artificial Sequence

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<220>

<223> 3' Primer is a synthetic anti-sense-strand oligonucleotide encoding amino acid 43-59 of the VH region (SEQ ID No. 2). The primer overlaps with the template by 21 nucleotides.

<220>

<221> primer_bind

<222> (1)..(48)

<223>

<400> 5
gtaggtggtgta ccaccaccac tactaatgta tgcgaccac tccagccc . 48

<210> 6

<211> 132

<212> DNA

<213> Artificial Sequence

<220>

<223> C-terminal is a synthetic sense-strand oligonucleotide encoding amino acid 68-111 of the VH region (SEQ ID No 2) The template is PCR-amplified by two primers (SEQ ID No 7 and 8)

<220>

<221> V_region

<222> (1)..(132)

<223>

<400> 6
ttcaccatct ccagagacaa tgccaagaac tccctgtacc tgcaaatgaa cagtctgagg 60
gtggaggaca cagccttata ttactgtgca agacatagtg gctacggtag tagctacggg 120
gttttggttg ct 132

<210> 7

<211> 60

<212> DNA

<213> Artificial Sequence

<220>

<223> 5' Primer is a synthetic sense-strand oligonucleotide encoding amino acid 55-74 of the VH region (SEQ ID No 2). The 3' end of the primer overlaps with the 5' end of the template by 21 nucleotides

<220>

<221> primer_bind

<222> (1)..(60)

<223>

<400> 7

ggtggtacca cctactatcc agacactgtg aagggccgat tcaccatctc cagagacaat 60

<210> 8

<211> 57

<212> DNA

<213> Artificial Sequence

<220>

<223> 3' Primer is a synthetic anti-sense-strand oligonucleotide encoding amino acid 105-123 of the VH region (SEQ ID No 2). The primer and the template overlaps by 21 nucleotides.

<220>

<221> primer_bind

<222> (1)..(57)

<223>

<400> 8

tgaagagaca gtgaccagag tcccttgGCC ccagtaagca aacaaaaccc cgtagct 57

<210> 9

<211> 321

<212> DNA

<213> Artificial Sequence

<220>

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<223> FR-patched light chain variable region sequence formed by joining the N- and C- terminal (SEQ 11 and 14) halves at the KpeI site.

<220>

<221> V_region

<222> (1)..(321)

<223>

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ggtaaggctc cgaaactcct gatctactac actagtatat tacactcagg agtcccatca 180
aggttcagtg gcagtgggtc tggaacagaa tttactctca ccattagctc cctgcagcca 240
gaagattttg ccacttactt ttgccaacag ggtaatacgc ttccgtggac gttcgggtgga 300
ggcaccaagg tggaatcaa a 321

<210> 10

<211> 107

<212> PRT

<213> Chimaera sp.

<400> 10

Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15
Asp Arg Val Thr Ile Ser Cys Arg Ala Ser Gln Asp Ile Ser Asn Tyr
20 25 30
Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
35 40 45
Tyr Tyr Thr Ser Ile Leu His Ser Gly Val Pro Ser Arg Phe Ser Gly
50 55 60
Ser Gly Ser Gly Thr Glu Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65 70 75 80
Glu Asp Phe Ala Thr Tyr Phe Cys Gln Gln Gly Asn Thr Leu Pro Trp
85 90 95

Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
 100 105

<210> 11

<211> 108

<212> DNA

<213> Artificial Sequence

<220>

<223> N-template is a synthetic sense-strand oligonucleotide encoding a
 amino acid 11-46 of the VL region (SEQ ID No. 10). The template is
 PCR-amplified by two primers (SEQ ID No. 12 and 13)

<220>

<221> V_region

<222> (1)..(108)

<223>

<400> 11

ctgtctgcct ctgtgggaga cagagtcacc attagttgca gggcaagtca ggacattagc 60
 aattatttaa actggtatca gcagaaacca ggtaaggctc cgaaactc 108

<210> 12

<211> 51

<212> DNA

<213> Artificial Sequence

<220>

<223> 5' Primer is a synthetic sense-strand oligonucleotide encoding am
 ino acid 1-17 of the VH region (SEQ ID No 10). The 3' end of the
 primer overlaps with the 5'end of the template by 21 nucleotides

<220>

<221> primer_bind

<222> (1)..(51)

<223>

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<400> 12
gatatccaga tgaccagtc tccatcctcc ctgtctgcct ctgtgggaga c 51

<210> 13

<211> 40

<212> DNA

<213> Artificial Sequence

<220>

<223> 3' Primer is a synthetic anti-sense-strand oligonucleotide encoding amino acid 40-53. The primer and the template overlaps by 18 nucleotides.

<220>

<221> primer_bind

<222> (1)..(40)

<223>

<400> 13
atatactagt gtagtagatc aggagtttcg gaggccttacc 40

<210> 14

<211> 120

<212> DNA

<213> Artificial Sequence

<220>

<223> C-terminal is a synthetic sense-strand oligonucleotide encoding amino acid 59-98 of the VH region (SEQ ID No 10) The template is PCR-amplified by two primers (SEQ ID No 15 and 16)

<220>

<221> V_region

<222> (1)..(120)

<223>

<400> 14
ccatcaaggt tcagtggcag tgggtctgga acagaattta ctctcaccat tagctccctg 60

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cagccagaag attttgccac ttacttttgc caacagggtg atacgcttcc gtggacgttc 120

<210> 15

<211> 49

<212> DNA

<213> Artificial Sequence

<220>

<223> 5' Primer is a synthetic sense-strand oligonucleotide encoding amino acid 50-65 of the VH region (SEQ ID No. 10). The 3' end of the primer overlaps with the 5' end of the template by 21 nucleotides

<220>

<221> primer_bind

<222> (1)..(49)

<223>

<400> 15
ctacactagt atattacact caggagtccc atcaaggttc agtggcagt 49

<210> 16

<211> 48

<212> DNA

<213> Artificial Sequence

<220>

<223> 3' Primer is a synthetic anti-sense-strand oligonucleotide encoding amino acid 92-107 of the VH region (SEQ ID No 10). The primer and the template overlaps by 21 nucleotides.

<220>

<221> primer_bind

<222> (1)..(48)

<223>

<400> 16
tttgatttcc accttggtgc ctccaccgaa cgtccacgga agcgtatt 48

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<210> 17
 <211> 371
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> FR-patched heavy chain variable region sequence (Full DNA Sequence) formed by joining the N- and C- terminal (SEQ 19 and 22) halves at the KpeI site.
 <220>
 <221> V_region
 <222> (1)..(371)
 <223>

<400> 17
 caggtgcaac tgggtggcttc cggggctgag gtaaataagc ctggggcctc agtgaaggctc 60
 tcctgcaagg cttctggcta cacatttacc agttacaata tgcactgggt acggcagcct 120
 cctggaaggg gcctggaatg gattggagct atttatccag gaaatgggtga tactagttac 180
 aatcagaaat tcaagggcaa ggccacattg actgcagaca aatcctccag cacagcctac 240
 atgcagctca gcagtctgac atctgaggac tctgcggtct attactgtgc aagatcgcac 300
 tacggtagta actacgtaga ctactttgac tactggggcc aaggcaccac tgttacagtc 360
 tcctctgata a 371

<210> 18
 <211> 123
 <212> PRT
 <213> Chimaera sp.

<400> 18
 Gln Val Gln Leu Val Ala Ser Gly Ala Glu Val Asn Lys Pro Gly Ala
 1 5 10 15
 Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
 20 25 30

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Asn Met His Trp Val Arg Gln Pro Pro Gly Arg Gly Leu Glu Trp Ile
35 40 45

Gly Ala Ile Tyr Pro Gly Asn Gly Asp Thr Ser Tyr Asn Gln Lys Phe
50 55 60

Lys Gly Lys Ala Thr Leu Thr Ala Asp Lys Ser Ser Ser Thr Ala Tyr
65 70 75 80

Met Gln Leu Ser Ser Leu Thr Ser Glu Asp Ser Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Ser His Tyr Gly Ser Asn Tyr Val Asp Tyr Phe Asp Tyr Trp
100 105 110

Gly Gln Gly Thr Thr Val Thr Val Ser Ser Asp
115 120

<210> 19

<211> 114

<212> DNA

<213> Artificial Sequence

<220>

<223> N-template is a synthetic sense-strand oligonucleotide encoding a
mino acid 12-49 of the VH region (SEQ ID No. 18). The template i
s PCR-amplified by two primers (SEQ ID No. 20 and 21)

<220>

<221> V_region

<222> (1)..(114)

<223>

<400> 19

aataagcctg gggcctcagt gaaggtctcc tgcaaggctt ctggctacac atttaccagt 60
tacaatatgc actgggtacg gcagcctcct ggaaggggccc tggaatggat tgga 114

<210> 20

<211> 57

<212> DNA

<213> Artificial Sequence

<220>

<223> 5' Primer is a synthetic sense-strand oligonucleotide encoding amino acid 1-19 of the VH region (SEQ ID No 18). The 3' end of the primer overlaps with the 5' end of the template by 24 nucleotides

<220>

<221> primer_bind

<222> (1)..(57)

<223>

<400> 20
cagggtgcaac tgggtggcttc cggggctgag gtaaataagc ctggggcctc agtgaag 57

<210> 21

<211> 55

<212> DNA

<213> Artificial Sequence

<220>

<223> 3' Primer is a synthetic anti-sense-strand oligonucleotide encoding amino acid 43-60 of the VH region (SEQ ID No 18). The primer and the template overlaps by 21 nucleotides.

<220>

<221> primer_bind

<222> (1)..(55)

<223>

<400> 21
tgtaactagt atcaccattt cctggataaa tagctccaat ccattccagg cccct 55

<210> 22

<211> 126

<212> DNA

<213> Artificial Sequence

<220>

<223> C-terminal is a synthetic sense-strand oligonucleotide encoding a
mino acid 70-111 of the VH region (SEQ ID No 18) The template is
PCR-amplified by tow primers (SEQ ID No 23 and 24)

<220>

<221> V_region

<222> (1)..(126)

<223>

<400> 22

ttgactgcag acaaatcctc cagcacagcc tacatgcagc tcagcagtct gacatctgag 60

gactctgcgg tctattactg tgcaagatcg cactacggta gtaactacgt agactacttt 120

gactac 126

<210> 23

<211> 61

<212> DNA

<213> Artificial Sequence

<220>

<223> 5' Primer is a synthetic sense-strand oligonucleotide encoding am
ino acid 57-76 of the VH region (SEQ ID No 18). The 3' end of th
e primer overlaps with the 5'end of the template by 21 nucleotide
s.

<220>

<221> primer_bind

<222> (1)..(61)

<223>

<400> 23

tgatactagt tacaatcaga aattcaaggg caaggccaca ttgactgcag acaaatcctc 60

c 61

<210> 24

<211> 59

<212> DNA

<213> Artificial Sequence

<220>

<223> 3' Primer is a synthetic anti-sense-strand oligonucleotide encoding amino acid 105-123 of the VH region (SEQ ID No 18). The primer and the template overlaps by 21 nucleotides.

<220>

<221> primer_bind

<222> (1)..(59)

<223>

<400> 24

tgatcagagg agactgtaac agtgggtgcct tggccccagt agtcaaagta gtctacgta	59
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<210> 25

<211> 321

<212> DNA

<213> Artificial Sequence

<220>

<223> FR-patched light chain variable region sequence (Full DNA Sequence) formed by joining the N- and C- terminal (SEQ 27 and 30) halves at the BspEI site.

<220>

<221> V_region

<222> (1)..(321)

<223>

<400> 25

gatattcaac tcacacagtc tccatcaagt ctttctgcat ctgtggggga cagagtcaca	60
attacttgca gggccagctc aagtttaagt ttcatgcact ggtaccagca gaagccagga	120
tcctcccca aaccctggat ttatgccaca tccaacctgg cttccggagt ccctagtcgc	180
ttcagtgga gtgggtctgg gaccgagttc actctcaca tcagcagttt gcagcctgaa	240
gatttcgca cttatttctg ccatcagtg agtagtaacc cgctcacgtt cggtgctggg	300

accaagctga ccgttctacg g

<210> 26

<211> 107

<212> PRT

<213> Chimaera sp.

<400> 26

Asp Ile Gln Leu Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Ser Ser Leu Ser Phe Met
20 25 30

His Trp Tyr Gln Gln Lys Pro Gly Ser Ser Pro Lys Pro Trp Ile Tyr
35 40 45

Ala Thr Ser Asn Leu Ala Ser Gly Val Pro Ser Arg Phe Ser Gly Ser
50 55 60

Gly Ser Gly Thr Glu Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu
65 70 75 80

Asp Phe Ala Thr Tyr Phe Cys His Gln Trp Ser Ser Asn Pro Leu Thr
85 90 95

Phe Gly Ala Gly Thr Lys Leu Thr Val Leu Arg
100 105

<210> 27

<211> 129

<212> DNA

<213> Artificial Sequence

<220>

<223> N-template is a synthetic sense-strand oligonucleotide encoding a
mino acids 9-51 of the VL region (SEQ ID No. 26). The template is
PCR-amplified by two primers (SEQ ID No. 28 and 29).

<220>

<221> V_region

<222> (1)..(129)

<223>

<400> 27

tcaagtcttt ctgcatctgt gggggacaga gtcacaatta cttgcagggc cagctcaagt 60

ttaagtttca tgcactggta ccagcagaag ccaggatcct cccccaaacc ctggatttat 120

gccacatcc 129

<210> 28

<211> 45

<212> DNA

<213> Artificial Sequence

<220>

<223> 5' Primer is a synthetic sense-strand oligonucleotide encoding amino acid 1-15 of the VH region (SEQ ID No 26). The 3' end of the primer overlaps with the 5' end of the template by 21 nucleotides

<220>

<221> primer_bind

<222> (1)..(45)

<223>

<400> 28

gatattcaac tcacacagtc tccatcaagt ctttctgcat ctgtg 45

<210> 29

<211> 40

<212> DNA

<213> Artificial Sequence

<220>

<223> 3' Primer is a synthetic anti-sense-strand oligonucleotide encoding amino acid 45-57. The primer and the template overlaps by 21 nucleotides.

<220>

<221> primer_bind

<222> (1)..(40)

<223>

<400> 29

ggactccgga agccagggtg gatgtggcat aaatccaggg

40

<210> 30

<211> 120

<212> DNA

<213> Artificial Sequence

<220>

<223> C-terminal is a synthetic sense-strand oligonucleotide encoding a
mino acid 61-100 of the VH region (SEQ ID No 26) The template is
PCR-amplified by tow primers (SEQ ID No 31 and 32)

<220>

<221> V_region

<222> (1)..(120)

<223>

<400> 30

ttcagtggca gtgggtctgg gaccgagttc actctcacia tcagcagttt gcagcctgaa 60

gatttcgcca cttatttctg ccatcagtgg agtagtaacc cgctcacgtt cggtgctggg 120

<210> 31

<211> 43

<212> DNA

<213> Artificial Sequence

<220>

<223> 5' Primer is a synthetic sense-strand oligonucleotide encoding am
ino acid 54-67 of the VH region (SEQ ID No 18). The 3' end of th
e primer overlaps with the 5'end of the template by 21 nucleotide
s.

<220>

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<221> primer_bind

<222> (1)..(43)

<223>

<400> 31

ggcttccgga gtccttagtc gcttcagtgg cagtgggtct ggg

43

<210> 32

<211> 42

<212> DNA

<213> Artificial Sequence

<220>

<223> 3' Primer is a synthetic anti-sense-strand oligonucleotide encoding amino acid 94-107 of the VH region (SEQ ID No 26). The primer and the template overlaps by 21 nucleotides.

<220>

<221> primer_bind

<222> (1)..(42)

<223>

<400> 32

ccgtagaacg gtcagcttgg tcccagcacc gaacgtgagc gg

42